This Listing of Claims will replace all prior versions, and listings, of claims in the application:

Listing of the Claims

1. (currently amended) A humanized antibody that binds specifically to human tissue factor (TF) to form a complex, wherein factor X or factor IX binding to the complex and the FX or FIX activation by TF:FVIIa are inhibited, wherein,

each of frameworks (FRs) 1, 2, 3 and 4 of the humanized antibody has at least about 90% amino acid sequence identity to any one of the light chain FR sequences shown in Figure 12A (SEQ ID NOS. 73-82), or

each of frameworks (FRs) 1, 2, 3 and 4 of the humanized antibody has at least about 90% amino acid sequence identity to any one of the heavy chain sequences shown in Figure 13A (SEQ ID NOS. 84-96),

wherein the antibody has a dissociation constant (K_d) for the TF of less than about 0.5 nM or it increases blood clotting time by at least about 5 seconds as determined by a standard prothrombin (PT) clotting assay at an antibody concentration of < 15 nM.

2-4. (canceled)

5. (currently amended) The humanized antibody of claim 1 ~~or 2~~, wherein the antibody has a dissociation constant (K_d) for the TF about equal to or greater than the antibody obtained from cell line H36.D2.B7 deposited under ATCC Accession No. HB-12255.

6. (currently amended) The humanized antibody of claim 1 ~~or 2~~, wherein the antibody comprises at least one fully murine complimentarity determining region (CDR).

7. (currently amended) The humanized antibody of claim 1 ~~or 6~~, wherein the antibody comprises at least one fully human framework (FR) region.

8. (original) The humanized antibody of claim l, wherein the antibody has at least about 90% amino acid sequence identity to a human antibody.

9. (original) The humanized antibody of claim 1, wherein the variable region of the humanized antibody has at least about 70% amino acid sequence identity to a human antibody variable region.

10. canceled.

11. (currently amended) The humanized antibody of claim 1, wherein the antibody comprises a light chain constant region having at least about 95% amino acid sequence identity to the sequence shown in Figure 14A or 15A (SEQ ID NO. 97 or ~~98~~ 99).

12. canceled.

13. (currently amended) The humanized antibody of claim 11 ~~12~~, wherein the antibody further comprises a heavy chain constant region having at least about 95% amino acid sequence identity to sequence shown in Figure 14B or 15B (SEQ ID NO. 97 or 100).

14. (original) The humanized antibody of claim 1, wherein the antibody has an IgG1 (hOAT) or IgG4 (hFAT) isotype.

15. (original) A human TF binding fragment of the humanized antibody of claim 1.

16. (original) The human TF binding fragment of claim 15, wherein the fragment is Fab, Fab', or $F(ab)_2$.

17. (currently amended) A humanized antibody comprising at least one murine complementarity determining region (CDR), wherein the antibody binds specifically to human tissue factor (TF) to form a complex, and further wherein factor X or factor IX binding to TF or TF:FVIIa and activation by TF:FVIIa thereto is inhibited wherein,

each of frameworks (FRs) 1, 2, 3 and 4 of the humanized antibody has at least about 90% amino acid sequence identity to any one of the light chain FR sequences shown in Figure 12A (SEQ ID NOS. 73-82), or

each of frameworks (FRs) l, 2, 3 and 4 of the humanized antibody has at least about 90% amino acid sequence identity to any one of the heavy chain sequences shown in Figure 13A (SEQ ID NOS. 84-96) and further wherein the antibody has a dissociation constant (K_d) for the TF of less than about 0.5 nM or it increases blood clotting time by at least about 5 seconds as determined by a standard prothrombin (PT) clotting assay at an antibody concentration of < 15 nM.

18. (original) The humanized antibody of claim 17, wherein all the CDR (light and heavy chain) are murine.

19. (previously presented) The humanized antibody of claim 17, wherein the antibody comprises at least one human framework (FR) region.

20. (original) The humanized antibody of claim 19, wherein the amino acid sequences of all the FR (light and heavy chain) are human or within 2 amino acid substitutions of being human.

21. (previously presented) The humanized antibody of claim 17, wherein the first CDR (CDR1) of the heavy chain hypervariable region is at least 95% identical to the CDR1 amino acid sequence shown in Figure 13B (SEQ ID NO. 8).

22. (previously presented) The humanized antibody of claim 17, wherein the second CDR (CDR2) of the heavy chain hypervariable region is at least 95% identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or 101).

23. (previously presented) The humanized antibody of claim 17, wherein the third CDR (CDR3) of the heavy chain hypervariable region is at least 95% identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10).

24. (previously presented) The humanized antibody of claim 17, wherein the first CDR (CDR1) of the light chain hypervariable region is at least 95% identical to the CDR1 amino acid sequence shown in Figure 12B (SEQ ID NO.2).

25. (previously presented) The humanized antibody of claim 17, wherein the second CDR (CDR2) of the light chain hypervariable region is at least 95% identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6).

26. (previously presented) The humanized antibody of claim 17, wherein the third CDR (CDR3) of the light chain hypervariable region is at least 95% identical to the CDR3 amino acid sequence shown in Figure 12D (SEQ ID NO. 7).

27-42. canceled

43. (original) A human TF binding fragment of the humanized antibody of claim 17.

44. (original) The human TF binding fragment of claim 43, wherein the fragment is Fab, Fab', or $F(ab)_2$.

45. (currently amended) A humanized antibody comprising ~~at least one~~ three ~~murine~~ complementarity determining regions (CDRs), wherein the antibody binds specifically to

human tissue factor (TF) to form a complex, and further wherein factor X or factor IX binding to TF or TF:FVIIa and activation by TF:FVIIa thereto is inhibited, the antibody comprising on the heavy chain:

a) a first CDR (CDR1) which is at least 95% identical to CDR1 amino acid sequence shown in Figure 13B (SEQ ID NO. 8),

b) a second CDR (CDR2) which is at least 95% identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or 101),

c) a third CDR (CDR3) which is at least 95% identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10),

d) a first framework (FR1) which is at least 95% identical to the FR1 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

e) a second framework (FR2) which is at least 95% identical to the FR2 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

f) a third framework (FR3) which is at least 95% identical to the FR3 amino acid sequence shown in Figure 12A (SEQ ID NO. 79), and

g) a fourth framework (FR4) which is at least 95% identical to the FR4 amino acid sequence shown in Figure 12A (SEQ ID No. 79), wherein the antibody has a dissociation constant (K_d) for the TF of less than about 0.5 nM or it increases blood clotting time by at least about 5 seconds as determined by a standard prothrombin (PT) clotting assay at an antibody concentration of < 15 nM.

46. (currently amended) The antibody of claim 45, wherein the light chain comprises,

h) a first CDR (CDR1) which is at least 95% identical to CDR1 amino acid sequence shown in Figure 12B (SEQ ID NO. 2),

i) a second CDR (CDR2) which is at least 95% identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),

j) a third CDR (CDR3) which is at least 95% identical to the CDR3 amino acid

sequence shown in Figure ~~12C~~ 12D (SEQ ID NO. ~~6~~ 7),

k) a first framework (FR1) which is at least 95% identical to the FR1 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

l) a second framework (FR2) which is at least 95% identical to the FR2 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

m) a third framework (FR3) which is at least 95% identical to the FR3 amino acid sequence shown in Figure 12A (SEQ ID NO. 79), and

n) a fourth framework (FR4) which is at least 95% identical to the FR4 amino acid sequence shown in Figure 12A (SEQ ID NO. 79), wherein the antibody has a dissociation constant (K_d) for the TF of less than about 0.5 nM or it increases blood clotting time by at least about 5 seconds as determined by a standard prothrombin (PT) clotting assay at an antibody concentration of < 15 nM.

47. (previously presented) The antibody of claim 45, wherein the light chain comprises the constant sequence of Figure 14A (SEQ ID NO. 97) or Figure 15A (SEQ ID NO. 99).

48. (previously presented) The antibody of claim 45 further comprising the heavy chain constant region of Figure 14B (SEQ ID NO. 98) or Figure 15B (SEQ ID NO.100)

49. (original) A human TF binding fragment of the humanized antibody of claim 45.

50. (original) The human TF binding fragment of claim 45, wherein the fragment is Fab, Fab', or $F(ab)_2$.

51. (previously presented) A humanized antibody comprising on the heavy chain:

a) a first CDR (CDR1) identical to the CDR1 amino acid sequence shown in Figure 13B (SEQ ID NO. 8),

b) a second CDR (CDR2) identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or 101),

c) a third CDR (CDR3) identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10),

d) a first framework (FR1) identical to the FR1 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

e) a second framework (FR2) identical to the FR2 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

f) a third framework (FR3) identical to the FR3 amino acid sequence shown in Figure 13A (SEQ ID NO. 91); and

g) a fourth framework (FR4) identical to the FR4 amino acid sequence shown in Figure 13A (SEQ ID No. 91); and

on the light chain:

h) a first CDR (CDR1) identical to CDR1 amino acid sequence shown in Figure 12B (SEQ ID NO. 2),

i) a second CDR (CDR2) identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),

j) a third CDR (CDR3) identical to the CDR3 amino acid sequence shown in Figure 12D (SEQ ID NO. 7),

k) a first framework (FR1) identical to the FR1 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

l) a second framework (FR2) identical to the FR2 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

m) a third framework (FR3) identical to the FR3 amino acid sequence shown in Figure 12A (SEQ ID NO. 79), and

n) a fourth framework (FR4) identical to the FR4 amino acid sequence shown in Figure 12A (SEQ ID NO. 79).

52. (previously presented) The antibody of claim 51, wherein the light chain comprises constant sequence of Figure 14A (SEQ ID NO. 97) or Figure 15A (SEQ ID NO. 99).

53. (previously presented) The antibody of claim 51 further comprising the heavy chain constant sequence of Figure 14B (SEQ ID NO. 98) or 15B (SEQ ID NO.100).

54. (original) The humanized antibody of claim 51, wherein the antibody has an IgG1 or IgG4 isotype.

55. (original) A human TF binding fragment of the humanized antibody of claim 4.

56. (original) The human TF binding fragment of claim 55, wherein the fragment is Fab, Fab', or $F(ab)_2$.

57. (original) The humanized antibody of claim 1, wherein the antibody is a monoclonal antibody.

58. (original) A single-chain antibody comprising the hypervariable region of the antibody of claim 1.

Claims 59-61 (Canceled)

62. (original) A composition comprising the humanized antibody of claim 1, and at least one pharmaceutically acceptable carrier.

Claims 63-72 (Canceled)

73. (previously presented) The humanized antibody of claim 6, wherein the antibody comprises at least one fully human framework (FR) region.

74. (previously presented) A humanized antibody comprising on the heavy chain:

a) a first CDR (CDR1) identical to the CDR1 amino acid sequence shown in Figure 13B (SEQ ID NO. 8),

b) a second CDR (CDR2) identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or 101),

c) a third CDR (CDR3) identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10),

d) a first framework (FR1) identical to the FR1 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

e) a second framework (FR2) identical to the FR2 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

f) a third framework (FR3) identical to the FR3 amino acid sequence shown in Figure 13A (SEQ ID NO. 91); and

g) a fourth framework (FR4) identical to the FR4 amino acid sequence shown in Figure 13A (SEQ ID No. 91); and

on the light chain:

h) a first CDR (CDR1) identical to CDR1 amino acid sequence shown in Figure 12B (SEQ ID NO. 2),

i) a second CDR (CDR2) identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),

j) a third CDR (CDR3) identical to the CDR3 amino acid sequence shown in Figure 12D (SEQ ID NO. 7),

k) a first framework (FR1) identical to the FR1 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

l) a second framework (FR2) identical to the FR2 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

m) a third framework (FR3) identical to the FR3 amino acid sequence shown in Figure 12A (SEQ ID NO. 79), and

n) a fourth framework (FR4) identical to the FR4 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

wherein, the humanized antibody further comprising a light chain constant sequence identical to the sequence of Figure 14A (SEQ ID NO. 97) or Figure 15A (SEQ ID NO. 99), the humanized antibody further comprising the heavy chain constant sequence of Figure 14B (SEQ ID NO. 98) or 15B (SEQ ID NO.100),

and further wherein, the humanized antibody has an IgG1(hOAT) or IgG4 (hFAT) isotype.

75. (new) A humanized antibody comprising at least one murine complementarity determining region (CDR), wherein the antibody binds specifically to human tissue factor (TF) to form a complex, and further wherein factor X or factor IX binding to TF or TF:FVIIa and activation by TF:FVIIa thereto is inhibited wherein, wherein,

(i) each of frameworks (FRs) 1, 2, 3 and 4 of the humanized antibody has at least about 90% amino acid sequence identity to any one of the light chain FR sequences shown in Figure 12A (SEQ ID NOS. 73-82), and

(ii) FR1 of the heavy chain hypervariable region is as shown in Figure 13A (SEQ ID NO. 83), the region further comprising at least one of the following amino acid changes: El to Q; Q5 to V; P9 to G; L11 to V; V12 to K; Q19 to R; and T24 to A; and

further wherein the antibody has a dissociation constant (K_d) for the TF of less than about 0.5 nM or it increases blood clotting time by at least about 5 seconds as

determined by a standard prothrombin (PT) clotting assay at an antibody concentration of < 15 nM.

76. (new) A humanized antibody comprising at least one murine complementarity determining region (CDR), wherein the antibody binds specifically to human tissue factor (TF) to form a complex, and further wherein factor X or factor IX binding to TF or TF:FVIIa and activation by TF:FVIIa thereto is inhibited wherein, wherein,

(i) each of frameworks (FRs) 1, 2, 3 and 4 of the humanized antibody has at least about 90% amino acid sequence identity to any one of the light chain FR sequences shown in Figure 12A (SEQ ID NOS. 73-82), and

(ii) FR2 of the heavy chain hypervariable region is shown in Figure 13A (SEQ ID NO. 83), the region further comprising at least one of the following amino acid changes: 41H to P; and 44S to G; and

further wherein the antibody has a dissociation constant (K_d) for the TF of less than about 0.5 nM or it increases blood clotting time by at least about 5 seconds as determined by a standard prothrombin (PT) clotting assay at an antibody concentration of < 15 nM.

77. (new) A humanized antibody comprising at least one murine complementarity determining region (CDR), wherein the antibody binds specifically to human tissue factor (TF) to form a complex, and further wherein factor X or factor IX binding to TF or TF:FVIIa and activation by TF:FVIIa thereto is inhibited wherein, wherein,

(i) each of frameworks (FRs) 1, 2, 3 and 4 of the humanized antibody has at least about 90% amino acid sequence identity to any one of the light chain FR sequences shown in Figure 12A (SEQ ID NOS. 73-82), and

(ii) FR3 of the heavy chain hypervariable region is shown in Figure 13A (SEQ ID NO. 83), the region further comprising at least one of the following amino acid changes: 76S to T; 77T to S; 80F to Y; 82H to E; 84N to S; 87T to R; 89D to E; and 91S to T; and

further wherein the antibody has a dissociation constant (K_d) for the TF of less than about 0.5 nM or it increases blood clotting time by at least about 5 seconds as

determined by a standard prothrombin (PT) clotting assay at an antibody concentration of < 15 nM.

78. (new) A humanized antibody comprising at least one murine complementarity determining region (CDR), wherein the antibody binds specifically to human tissue factor (TF) to form a complex, and further wherein factor X or factor IX binding to TF or TF:FVIIa and activation by TF:FVIIa thereto is inhibited wherein, wherein,

(i) each of frameworks (FRs) 1, 2, 3 and 4 of the humanized antibody has at least about 90% amino acid sequence identity to any one of the light chain FR sequences shown in Figure 12A (SEQ ID NOS. 73-82), and

(ii) FR4 of the heavy chain hypervariable region is shown in Figure 13A (SEQ ID NO. 83), the region further comprising the following amino acid change: 113L to V; and

further wherein the antibody has a dissociation constant (K_d) for the TF of less than about 0.5 nM or it increases blood clotting time by at least about 5 seconds as determined by a standard prothrombin (PT) clotting assay at an antibody concentration of < 15 nM.

79. (new) A humanized antibody comprising at least one murine complementarity determining region (CDR), wherein the antibody binds specifically to human tissue factor (TF) to form a complex, and further wherein factor X or factor IX binding to TF or TF:FVIIa and activation by TF:FVIIa thereto is inhibited wherein,

(i) the FR1 of the light chain is shown in Figure 12A (SEQ ID NO. 72), the chain comprising at least one of the following amino acid changes: 11QL to L; 15L to V; 17E to D and 18S to R; and

ii) each of frameworks (FRs) l, 2, 3 and 4 of the humanized antibody has at least about 90% amino acid sequence identity to any one of the heavy chain sequences shown in Figure 13A (SEQ ID NOS. 84-96) and further wherein the antibody has a dissociation constant (K_d) for the TF of less than about 0.5 nM or it increases

blood clotting time by at least about 5 seconds as determined by a standard prothrombin (PT) clotting assay at an antibody concentration of < 15 nM.

80. (new) A humanized antibody comprising at least one murine complementarity determining region (CDR), wherein the antibody binds specifically to human tissue factor (TF) to form a complex, and further wherein factor X or factor IX binding to TF or TF:FVIIa and activation by TF:FVIIa thereto is inhibited wherein,

(i) the FR2 of the light chain is shown in Figure 12A (SEQ ID NO. 72), the chain comprising the following amino acid change: 37Q to L; and

ii) each of frameworks (FRs) l, 2, 3 and 4 of the humanized antibody has at least about 90% amino acid sequence identity to any one of the heavy chain sequences shown in Figure 13A (SEQ ID NOS. 84-96) and further wherein the antibody has a dissociation constant (K_d) for the TF of less than about 0.5 nM or it increases blood clotting time by at least about 5 seconds as determined by a standard prothrombin (PT) clotting assay at an antibody concentration of < 15 nM.

81. (new) A humanized antibody comprising at least one murine complementarity determining region (CDR), wherein the antibody binds specifically to human tissue factor (TF) to form a complex, and further wherein factor X or factor IX binding to TF or TF:FVIIa and activation by TF:FVIIa thereto is inhibited wherein,

(i) the FR3 of the light chain is shown in Figure 12A (SEQ ID NO. 72), the chain comprising at least one of the following amino acid changes: 70K to D, 74K to T, 80A to P, 84V to A, and 85N to T; and

ii) each of frameworks (FRs) l, 2, 3 and 4 of the humanized antibody has at least about 90% amino acid sequence identity to any one of the heavy chain sequences shown in Figure 13A (SEQ ID NOS. 84-96) and further wherein the antibody has a dissociation constant (K_d) for the TF of less than about 0.5 nM or it increases blood clotting time by at least about 5 seconds as determined by a standard prothrombin (PT) clotting assay at an antibody concentration of < 15 nM.

82. (new) A humanized antibody comprising at least one murine complementarity determining region (CDR), wherein the antibody binds specifically to human tissue factor (TF) to form a complex, and further wherein factor X or factor IX binding to TF or TF:FVIIa and activation by TF:FVIIa thereto is inhibited wherein,

(i) the FR4 of the light chain is shown in Figure 12A (SEQ ID NO. 72), the chain comprising at least one of the following amino acid changes: 100A to Q; and 106L to I; and

ii) each of frameworks (FRs) 1, 2, 3 and 4 of the humanized antibody has at least about 90% amino acid sequence identity to any one of the heavy chain sequences shown in Figure 13A (SEQ ID NOS. 84-96) and further wherein the antibody has a dissociation constant (K_d) for the TF of less than about 0.5 nM or it increases blood clotting time by at least about 5 seconds as determined by a standard prothrombin (PT) clotting assay at an antibody concentration of < 15 nM.